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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/920,491	07/31/2001	Shoulian Dong	3417	1435

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AFFYMETRIX, INC
ATTN: CHIEF IP COUNSEL, LEGAL DEPT.
3380 CENTRAL EXPRESSWAY
SANTA CLARA, CA 95051

EXAMINER	
LU, FRANK WEI MIN	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 12/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/920,491	DONG, SHOULIAN	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 May 2004* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20,22,24-33,35-40 and 42-47* is/are pending in the application.

4a) Of the above claim(s) *28,32,42,44,45 and 47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20,22,24-27,29-31,33,35-40,43 and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

1. Applicant's response to the office action filed on August 12, 2004 has been entered. The claims pending in this application are claims 20, 22, 24-33, 35-40, and 42-47 wherein claims 28, 32, 42, 44, 45, and 47 have been withdrawn due to species election. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of amendment filed on August 12, 2004. Therefore, claims 20, 22, 24-27, 29-31, 35-40, 43, and 46 will be examined.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 25-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. Claims 25, 29, and 33 recite the limitation "the adaptor-ligated fragments" in the amplifying step of these claims. There is insufficient antecedent basis for this limitation in these claims since there is no phrase "adaptor-ligated fragments" in the fragmenting and ligating steps of these claims. Please clarify.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 20, 22, 24-27, 33, 40, 43, and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over McCasky Feazel *et al.*, (US Patent No. 6,100,030, filed on January 1998, priority date: January 1997) in view of Pedersen (US 2003/0113737 A1, priority date: February 12, 2001).

Regarding claims 20 and 25, McCasky Feazel *et al.*, teach method of mapping a polymorphic genetic marker, comprising the steps of: (i) providing a mixture of restriction enzyme-digested nucleic acids from biological samples; (ii) amplifying the mixture of restriction enzyme-digested nucleic acids; (iii) identifying a set of differentially amplified nucleic acids in the mixture; and, (iv) mapping at least one of the differentially amplified nucleic acids to a unique genetic polymorphism, thereby providing a marker for the polymorphism (see column

54, claim 15). Since McCasky Feazel *et al.*, teach providing a mixture of restriction enzyme digested nucleic acid from biological samples by double digestion of the nucleic acid with EcoR I and Mse I, ligating the mixture of restriction enzyme digested nucleic acid with an EcoR I adapter and a Mse I adapter and amplifying the ligation product of digested nucleic acids (see Figure 1 and claim 15 in column 54), McCasky Feazel *et al.*, disclose fragmenting a nucleic acid sample using a first and a second restriction enzyme to produce fragments, ligating a first and a second adaptor to the fragments to produce adaptor-ligated fragments wherein the first adaptor ligates to fragments cut by the first restriction enzyme and the second adaptor ligates to the fragments cut by the second restriction enzyme and amplifying the adaptor-ligated fragments to produce amplified fragments as recited in claims 20 and 25. Since McCasky Feazel *et al.*, teach an array of selection probes comprising polymorphic nucleotides and mapping polymorphic genetic marker or selection of polymorphic variants from the nucleic acid sample by hybridizing the amplified ligated products to the array (see claim 9 in column 53, claim 15 in column 54, claims 24 and 32 in column 32, and claim 47 in column 56), McCasky Feazel *et al.*, disclose providing a nucleic acid array consisting essentially of probes designed to detect polymorphisms predicted to be presented on the amplified fragments, hybridizing the amplified fragments to the array, and analyzing a hybridization pattern resulting from the hybridization or generating a hybridization pattern resulting from the hybridization or/and determining the polymorphisms in the individual based upon an analysis of the hybridization pattern as recited in claims 20 and 25.

Regarding claim 24, since McCasky Feazel *et al.*, teach to hybridize probes to amplification mixture, scan image of hybridization signal, and output scanning data (see Figure

11), McCasky Feazel *et al.*, must disclose that the polymorphisms predicted to be present in the amplified fragments are first determined by a computer system as recited in claim 24.

Regarding claims 22 and 26, since McCasky Feazel *et al.*, defines "polymorphism" as a change or difference between two related nucleic acids and defines "nucleotide polymorphism" as a nucleotide which is different in one sequence when compared to a related sequence when the two nucleic acids are aligned for maximal correspondence (see column 6, second paragraph), the polymorphisms taught by McCasky Feazel *et al.*, include SNP as recited in claims 22 and 26.

Regarding claim 27, since the nucleotide polymorphisms taught by McCasky Feazel *et al.*, are used as genetic markers for disease resistance loci (see column 33, second paragraph), McCasky Feazel *et al.*, disclose that the SNP is associated with a disease as recited in claim 27.

Regarding claim 33, since McCasky Feazel *et al.*, teach providing a mixture of restriction enzyme digested nucleic acid from biological samples by double digestion of the nucleic acid with EcoR I and Mse I, ligating the mixture of restriction enzyme digested nucleic acid with an EcoR I adapter and a Mse I adapter and amplifying the ligation product of digested nucleic acids (see Figure 1 and claim 15 in column 54), the nucleic acid and the amplified product are a first nucleic acid and a second nucleic acid sample as recited in claim 29. Since claim 29 and claim 20 have the same method steps, McCasky Feazel *et al.*, disclose providing a first nucleic acid sample from the individual; providing a second nucleic acid sample by: fragmenting the first nucleic acid sample using a first and second restriction enzyme to produce fragments wherein a collection of polymorphisms is predicted to be present in the fragments cut on one end by the first restriction enzyme and on the other end by the second restriction enzyme; ligating a fist and a second adaptor to the fragments wherein the first adaptor ligates to fragments cut by the first

restriction enzyme and the second adaptor ligates to the fragments cut by the second restriction enzyme; and amplifying the adaptor-ligated fragments to produce amplified fragments, hybridizing the second nucleic acid sample to an array designed to determine the bases present at one or more polymorphisms present in the collection of polymorphisms; generating a hybridization pattern resulting from the hybridizations; and determining the base present at one or more polymorphisms present in the collection of polymorphisms as recited in claim 33.

Regarding claim 40, since McCasky Feazel *et al.,* teach that the nucleic acid sample is cDNA or genomic DNA (see claim 17 in column 54), claim 40 is anticipated by McCasky Feazel *et al.*.

McCasky Feazel *et al.,* do not disclose that the first adaptor is blocked from ligation to the fragments at the 3' end of one stand of the first adaptor and the second adaptor is blocked from ligation to the fragments at the 5' end of one strand of the second adaptor as recited in claims 20, 25, and 29, one of the ligations is blocked by the absence of a phosphate at the 5' end of an adaptor strand as recited in claim 43, and one of the ligation is blocked at the 5' end of one strand of one adaptor and at the 3' end of one strand of the other adaptor as recited in claim 46.

Pedersen teaches assay and kit for analyzing gene expression.

Regarding claims 20, 25, and 33, since Pedersen teaches that linkers are blocked in any end of the two DNA strands by substituting the 5' PO_4 group or the 3' OH group with a blocking agent that prevents the ligation of the group to another nucleotide (see [0268]), it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use a first and a second adaptors wherein the first adaptor is blocked from ligation to the fragments at the 3' end of one stand of the first adaptor and the second adaptor is blocked from

ligation to the fragments at the 5' end of one strand of the second adaptor as recited in claims 20, 25, and 29 so that the ligation of the second adaptor is blocked by the absence of a phosphate at the 5' end of an adaptor strand of the second adaptor as recited in claim 43 and ligation of the second adaptor is blocked at the 5' end of one strand of the second adaptor and ligation of the first adaptor is blocked at the 3' end of one strand of the first adaptor as recited in claim 46.

Since EcoR I/Mse I double digested nucleic acids taught by McCasky Feazel *et al.*, comprise three types: (1) EcoR I digested nucleic acids (both ends with EcoR I cutting sites); (2) Mse I digested nucleic acids (both ends with Mse I cutting sites); and (3) EcoR I/ Mse I digested nucleic acids (one end with an EcoR I cutting site and another end with a Mse I cutting site) (see Figure 1A), when the first and second adaptors taught by McCasky Feazel *et al.*, are replaced by linkers or adaptors that are blocked in any end of the two DNA strands by substituting the 5' PO_4 group or the 3' OH group with a blocking agent taught by Pedersen, the most amplified product are fragments that are cut on one end by the first restriction enzyme (ie., EcoRI) and on the other end by the second restriction enzyme (ie., Mse I) (see Figure 1 of this instant application). Therefore, McCasky Feazel *et al.*, in view of Pedersen disclose that the adaptor-ligated fragments that are cut on one end by the first restriction enzyme (ie., EcoRI) and on the other end by the second restriction enzyme (ie., Mse I) and contain the first adaptor and the second adaptor are enriched in the amplification product relative to the adaptor-ligated fragments that are cut on both ends by the first restriction enzyme (ie., EcoRI or Mse I) and contain the first adaptor and do not contain the second adaptor or the adaptor-ligated fragments that are cut on both ends by the second restriction enzyme (ie., EcoRI or Mse I) and contain the second adaptor and do not contain the first adaptor as recited in claims 20, 25, and 33.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed in the methods recited in claims 20, 25, and 33 wherein the first adaptor is blocked from ligation to the fragments at the 3' end of one stand of the first adaptor and the second adaptor is blocked from ligation to the fragments at the 5' end of one strand of the second adaptor so that the adaptor-ligated fragments that are cut on one end by the first restriction enzyme (ie., EcoRI) and on the other end by the second restriction enzyme (ie., Mse I) and contain the first adaptor and the second adaptor are enriched in the amplification product relative to the adaptor-ligated fragments that are cut on both ends by the first restriction enzyme (ie., EcoRI or Mse I) and contain the first adaptor and do not contain the second adaptor or the adaptor-ligated fragments that are cut on both ends by the second restriction enzyme (ie., EcoRI or Mse I) and contain the second adaptor and do not contain the first adaptor in view of the prior art of McCasky Feazel *et al.*, and Pedersen. One having ordinary skill in the art would have been motivated to do so because the combination of two adaptors, one with blocked 3' end (3'-OH group) and another with blocked 5' end (5' -PO_4 group) in a ligation reaction recited in claims 20, 25, and 33 would prevent that the first adaptor ligates to the second adaptor and self-ligation of the first adaptor or the second adaptor (see Pedersen [0268]) so that the efficiency of the ligation reaction would be improved. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to perform the methods recited in claims 20, 25, and 33.

Response to Arguments

In page 10, third paragraph bridging to page 11, second paragraph of applicant's remarks, applicant argues that: (1) McCasky Feazel *et al.*, does not teach any method for preferentially

amplifying the fragments cut by both enzymes relative to the fragments cut only by one or the other enzyme"; and (2) Pederson fails to remedy the deficiencies of McCasky Feazel et al. Paragraph [0268] of Pederson teaches that 'identifying linker nucleotides' can be blocked from ligation at the 5' or 3' ends of either strand or both strands. There is no teaching or suggestion of blocking a first adaptor from ligation at the 3' end and a second adapter from ligation at the 5' end as required by the claims. The blocking of ligation of one adaptor at the 5' end and the other adaptor at the 3' end in the present invention allows for selective amplification of only those fragments that have both adaptors ligated to the ends of the fragments because only those fragments have a contiguous template strand containing both the first adaptor primer site and the second adaptor primer site. Neither Pederson nor McCasky Feazel teaches or suggests this limitation and it would not be prima facie obvious to one having ordinary skill in the art to have performed the methods recited in the claims in view of McCasky Feazel et al. and Pederson".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, although McCasky Feazel *et al.*, does not teach preferentially amplifying the fragments cut by both enzymes relative to the fragments cut only by one or the other enzyme, since Pedersen teaches that linkers are blocked in any end of the two DNA strands by substituting the 5' PO_4 group or the 3' OH group with a blocking agent that prevents the ligation of the group to another nucleotide (see [0268]), it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use a first and a second adaptors wherein the first adaptor is blocked from ligation to the fragments at the 3' end of one stand of the first adaptor and the second adaptor is blocked from ligation to the fragments at the 5' end of one strand of the second adaptor as recited in claims 20, 25, and 29 so that the

ligation of the second adaptor is blocked by the absence of a phosphate at the 5' end of an adaptor strand of the second adaptor as recited in claim 43 and ligation of the second adaptor is blocked at the 5' end of one strand of the second adaptor and ligation of the first adaptor is blocked at the 3' end of one strand of the first adaptor as recited in claim 46. Second, since EcoR I/Mse I double digested nucleic acids taught by McCasky Feazel *et al.*, comprise three types: (1) EcoR I digested nucleic acids (both ends with EcoR I cutting sites); (2) Mse I digested nucleic acids (both ends with Mse I cutting sites); and (3) EcoR I/ Mse I digested nucleic acids (one end with an EcoR I cutting site and another end with a Mse I cutting site) (see Figure 1A), when the first and second adaptors taught by McCasky Feazel *et al.*, are replaced by linkers or adaptors that are blocked in any end of the two DNA strands by substituting the 5' PO_4 group or the 3' OH group with a blocking agent taught by Pedersen, the most amplified product are fragments that are cut on one end by the first restriction enzyme (ie., EcoRI) and on the other end by the second restriction enzyme (ie., Mse I) (see Figure 1 of this instant application). Therefore, McCasky Feazel *et al.*, in view of Pedersen disclose that the adaptor-ligated fragments that are cut on one end by the first restriction enzyme (ie., EcoRI) and on the other end by the second restriction enzyme (ie., Mse I) and contain the first adaptor and the second adaptor are enriched in the amplification product relative to the adaptor-ligated fragments that are cut on both ends by the first restriction enzyme (ie., EcoRI or Mse I) and contain the first adaptor and do not contain the second adaptor or the adaptor-ligated fragments that are cut on both ends by the second restriction enzyme (ie., EcoRI or Mse I) and contain the second adaptor and do not contain the first adaptor as recited in claims 20, 25, and 33.

7. Claim 29-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over McCasky Feazel *et al.*, (1997) in view of Pedersen as applied to claims 20, 22, 24-27, 33, 40, 43, and 46 above, and further in view of Guire *et al.*, (US Patent No. 6,514,768 B1, filed on January 1999).

The teachings of McCasky Feazel *et al.*, and Pedersen have been summarized previously, *supra.* Since McCasky Feazel *et al.*, teach providing a mixture of restriction enzyme-digested nucleic acids from biological samples (see Figure 1 and claim 15 in column 54), McCasky Feazel *et al.*, disclose providing a first nucleic acid sample from each of the individuals as recited in claim 29 wherein the biological samples taught McCasky Feazel *et al.*, have two or more individuals. Except providing a plurality of identical nucleic acid arrays, claims 29 and 33 have the same method steps.

Regarding claims 30 and 31, since McCasky Feazel *et al.*, defines "polymorphism" as a change or difference between two related nucleic acids and defines "nucleotide polymorphism" as a nucleotide which is different in one sequence when compared to a related sequence when the two nucleic acids are aligned for maximal correspondence (see column 6, second paragraph), the polymorphisms taught by McCasky Feazel *et al.*, include SNP as recited in claim 30. Since the nucleotide polymorphisms taught by McCasky Feazel *et al.*, are used as genetic markers for disease resistance loci (see column 33, second paragraph), McCasky Feazel *et al.*, disclose that the SNP is associated with a disease as recited in claim 31.

McCasky Feazel *et al.*, and Pedersen do not teach to provide a plurality of identical nucleic acid arrays as recited in claim 29.

Guire *et al.*, teach replicable probe array. A plurality of identical nucleic acid arrays are made by a master nucleic acid array (see abstract, columns 3, and column 18, lines 42-53).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have provided a plurality of identical nucleic acid arrays during the process of practicing the method recited in claim 29 in view of the prior art of McCasky Feazel *et al.*, Pedersen and Guire *et al.*. One having ordinary skill in the art would have been motivated to do so because Guire *et al.*, have successfully produced a plurality of identical nucleic acid arrays from a master nucleic acid array and the availability of a plurality of identical nucleic acid arrays in a hybridization assay would let one having ordinary skill in the art at the time the invention was made to use the identical array for different purposes and save his or her time during the process for making a nucleic acid array. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to make a plurality of identical nucleic acid arrays during the process of practicing the method recited in claim 29.

Response to Arguments

In page 11, third paragraph of applicant's remarks, applicant argues that "[A]s discussed above McCasky Feazel et al. in view of Pederson fails to teach a method of selectively amplifying those fragments that are cut on one end by a first enzyme and on the other end by a second enzyme. Guire et al. fails to remedy the deficiencies of McCasky Feazel et a1. and Pederson".

This argument have been fully considered but it is not persuasive toward the withdrawal of the rejection because McCasky Feazel *et al.*, in view of Pederson do teach a method of selectively amplifying those fragments that are cut on one end by a first enzyme and on the other

end by a second enzyme (see Response to Arguments of the rejection on claims 20, 22, 24-27, 33, 40, 43, and 46 under 35 U.S.C 103 (a)).

8. Claims 35-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over McCasky Feazel *et al.,* (1997) in view of Pedersen as applied to claims 20, 22, 24-27, 33, 40, 43, and 46 above, and further in view of Short *et al.,* (US Patent NO. 6,238,884 B1, filed on May 9, 1999).

The teachings of McCasky Feazel *et al.,* and Pedersen have been summarized previously, *supra.*

McCasky Feazel *et al.,* and Pedersen do not teach that the adaptor-ligated fragments that contain both the first adaptor and the second adaptor comprise at least 0.01% to at least 30% of the nucleic acid sample as recited in claims 35-39.

Short *et al.,* teach that numbers of one kind of restriction enzyme site among different species are different (see column 56, first column).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed in the methods recited in claims 35-39 using nucleic acids from different species so that the adaptor-ligated fragments that contain both the first adaptor and the second adaptor comprise at least 0.01% to at least 30% of the nucleic acid sample in view of patents of McCasky Feazel *et al.,* Pedersen and Short *et al.*. One having ordinary skill in the art has been motivated to do so because optimization of source of nucleic acids in order to generate restriction fragments with yields as recited in claims 35-39, in the absence of convincing evidence to the contrary, would have been obvious to one having ordinary skill in the art at the time the invention was made. One having ordinary skill in the art at the time

the invention was made would have a reasonable expectation of success to generate restriction fragments with yields as recited in claims 35-39 by optimizing source of nucleic acids. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. Where the general conditions of a claim are disclosed in the prior art, it is not inventive, in the absence of an unexpected result, to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Response to Arguments

In page 11, last paragraph of applicant's remarks, applicant argues that "[A]s indicated above, McCasky Feazel et al. and Pederson fail to teach a method to preferentially amplify those fragments that are ligated to both a first and second adaptor relative to those fragments ligated to only the first adaptor or to only the second adaptor as required by amended claims 20, 25, 29 and 33. Short et al. also fail to teach a mechanism to preferentially amplify those fragments that are ligated to both a first adaptor and a second adaptor. Therefore, Short et al. fails to remedy the deficiencies of McCaskey Feazel et al. and Pederson".

This argument have been fully considered but it is not persuasive toward the withdrawal of the rejection because McCasky Feazel *et al.,* in view of Pederson do teach a method of method to preferentially amplify those fragments that are ligated to both a first and second adaptor relative to those fragments ligated to only the first adaptor or to only the second adaptor (see Response to Arguments of the rejection on claims 20, 22, 24-27, 33, 40, 43, and 46 under 35 U.S.C 103 (a)).

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10 No claim is allowed.

11. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (703)872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (571)272-0745.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
PSA
December 1, 2004

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
12/2/04